REMARKS

Claims 1- 4, 6, 9, 10, 20, 22 and 23 remain active in this application. Reconsideration is again respectfully requested.

Claim 20 is amended to correct an obvious inadvertent typographical error in the repetition of the phrase "in the composition" as kindly pointed out in the Final Office Action under reply. The amendment to Claim 20 obviates the rejection thereof under the second paragraph of 35 U.S.C. §112.

The rejection of Claims 1-4, 6, 10 and 20, under 35 U.S.C. §103 as being unpatentable over Lindmo *et al.* in view of Grange *et al.* is respectfully traversed. Although Applicants' arguments are not specifically addressed in the Final Office Action, it would appear that the previous rejection of these Claims as anticipated by Lindmo *et al.* under 35 U.S.C. §102 has been withdrawn in implicit recognition of the fact that Lindmo *et al.* cannot anticipate the claimed invention because it fails to enable an agglutination assay. This is respectfully submitted to be tacitly admitted in the Final Office Action wherein, after an extensive discussion of the similarities between the assay taught by Lindmo *et al.* and Applicants' assay as embodied in the Claims under consideration, it is admitted that Lindmo *et al.* fails to disclose that their first and second microparticles have a diameter from 30 to 600 nm so as to cause light scattering at wavelengths between 300 and 1200 nm. Therein lies the critical distinction.

Lindmo *et al.* discloses differential characterization between two microparticle populations, differential reactivity and dissociation constants between two immunological binding partners in flow cytometry applications, however it does <u>not</u> teach or suggest agglutination applications. Further, the particles taught by *Lindmo et al.*. are not colloidal but are "relatively large" (See *Lindmo et al.*, page 184, column 2), i.e. 7-10 μm in diameter, which renders them individually distinguishable by flow cytometry, but also renders them incapable of producing meaningful results in an agglutination assay as taught by Applicants. It is clear that, unlike the particles described by *Lindmo et al.*, the microparticles defined by the Claims are colloidal particles suitable for agglutination assays. Since the assay of *Lindmo et al.* is based on principles unrelated to those for which the claimed reagent is suitable, the person of ordinary

skill in the art would understand that the flow cytometry reagent disclosed in *Lindmo et al.* does not share the structural and functional characteristics of Applicants' claimed agglutination assay reagent.

In an effort to correct the deficiencies of Lindmo *et al.*, Grange *et al.*, previously withdrawn, has again been applied against the Claims. It is stated in the final Office Action under reply that it would have been obvious to one of ordinary skill in the art to generate microparticles in the size range of about 300 nm as taught by Grange *et al.* into the microparticles as taught by Lindmo *et al.* so as to enable detection of the microparticles in an agglutination assay because Grange *et al.* specifically taught that intensity of light scatter by a given suspension on microparticles if per chance used in an agglutination assay is dependent on the size and number of particles. It is respectfully submitted that one of ordinary skill in the art would not be in any way motivated to incorporate microparticles intended for use in a different assay based on different principles into the microparticles of Lindmo *et al.* on the mere chance that that the microparticles of Lindmo *et al.*, which are unsuited for an agglutination assay, might be tried in such an assay. It is respectfully submitted that this suggestion falls woefully short of motivation.

Grange *et al.* discloses the use of a microparticles at 300 nm being measured at wavelengths from 200 nm to 600 nm in an agglutination assay application, but fails to teach differential characterization between two microparticle populations. Grange *et al* also fails to teach differential reactivity and dissociation constants between two immunological binding partners. While the particle size taught by Grange et al. is essentially in the middle of the particle size range in the Claims under consideration, the upper limit to colloidal particle size range is commonly taken to be the size at which individual particles become visible in an optical (i.e., light) microscope (about 1 μm). Regardless of the discussion in the Final Office Action concerning particle size, agglutination assays are conducted with colloidal particles. The assay of Lindmo *et al.* is not an agglutination assay, operates on clearly different principles and utilizes non-colloidal particles (7-10μm) clearly outside the scope of Applicants' claims.

The statements in the Final Office Action under reply that one of ordinary skill in the art might want to include particles falling within the 200 nm to 600 nm range into the 7-10μm

microparticles taught by Lindmo *et al.* if per chance they might be utilized in an agglutination assay is at best a poor attempt at impermissible hindsight. The particles taught by Lindmo *et al.* are not suitable for an agglutination assay and diluting them with much finer microparticles will neither make them suitable for such an assay nor improve them for their original intended use. The continued addition of particles of the size taught by Grange to the particles of Lindmo *et al.* would eventually to detrimental to the purpose of the assay taught by Lindmo *et al.* which is based on the principles of flow cytometry. The person of ordinary skill in the art would understand that the flow cytometry reagent disclosed in Lindmo *et al.* does not share the structural and functional characteristics of the claimed agglutination assay reagent and would not by utilized by chance or design in an agglutination assay.

It is respectfully submitted that Lindmo *et al.* is rendered no more relevant to Applicants' Claims by Grange *et al.* than Grande *et al.* was when it was cited in view of Lindmo *et al.* earlier in the prosecution of the above-identified patent application. For the reasons fully stated in the record in Applicants' Brief on Appeal in this application Lindmo *et al.* and Grange *et al.* teach away from one another in that Lindmo *et al.* requires a reagent wherein relatively large particles remain monodispersed so that they can be individually detected by a flow cytometer and Grange *et al.* requires a reagent wherein relatively small microparticles aggregate to enhance their size and thus the light scattering properties of the immunological complexes into ranges detectable by nephelometry. There continues to be no teaching in the record upon which it can be established that one of ordinary skill in the art would be motivated to modify either Lindmo *et al.* or Grange *et al.* by the other to arrive at Applicants' invention. It is respectfully submitted that Claims 1-4, 6, 10 and 20 are clearly patentable over Lindmo *et al.* in view of Grange *et al.* Withdrawal of the rejection is therefore in order and is respectfully requested.

With regard to the specific rejection of Claim 4, it is respectfully submitted that Claim 4 is patentable for the reasons stated above. It is admitted on the record that neither Lindmo *et al.* nor Grange *et al.* teach the preferred range of relative diameter of Applicants' first microparticles to the second microparticles. This would be expected since the two citations, as presently combined, or as previously combined in the reverse order, fail to teach Applicants' reagent. Hence, Applicants are entitled to claim preferred embodiments, particularly when it is considered

that, since the citations do not motivate one of ordinary skill in the art to prepare Applicants' reagents, there is no way in which "routine experimentation" would have taken place, other than by an impermissible hindsight construction. Withdrawal of the rejection is in order and is respectfully requested.

The rejection of Claim 9 under 35 U.S.C. §103 as being unpatentable over Lindmo *et al.*. in view of Grange *et al.*, further in view of Sutton *et al.* is respectfully traversed. That Lindmo *et al.* and Grange *et al.* are not properly combinable and, in fact, teach away from Applicants' invention have been discussed above. Sutton *et al.* teaches specific copolymers coated on the surface of insoluble particles and having covalently bound thereto an oligonucleotide complimentary to a nucleic acid analyte. Such a teaching is respectfully submitted to be unrelated to the assay taught by Lindmo *et al.* and does not render Claim 9 unpatentable in combination with Grange *et al.* since it does not cure the deficiencies of Grange *et al.* as it would be applied to Claim 1. Therefore, based only on the fact that Sutton *et al.* teaches the use of oligonucleotide capture probes for a nucleic acid analyte, which is known in the art, it is respectfully submitted that one of ordinary skill in the art would not be led to create the reagent of Claim 9 by combining the teachings of Sutton *et al.* with Lindmo *et al.* and Grange *et al.* since their teachings are not combinable as pointed out above. Withdrawal of the rejection is respectfully requested.

The rejection of Claim 22 under 35 U.S.C. §103 as being unpatentable over Lindmo *et al.*. in view of Grange *et al.*, further in view of Collet-Cassart *et al.* is respectfully traversed. That Lindmo *et al.* and Grange *et al.* are not properly combinable and, in fact, teach away from Applicants' invention have been discussed above. Applicants respectfully take issue with the conclusionary statement that the combination of Lindmo *et al.* and Grange *et al.* differ from the invention as claimed in Claim 22 only in failing to teach that the analyte tested for is C-reactive (CRP) protein and that the immunological binding partners recognize different epitopes of the CRP protein. Collet-Cassart *et al*, in essence, teaches an improvement in agglutination assays wherein the analyte is CRP. The improvement is based on a competitive binding with particles that will agglutinate such that, by varying the concentration of a single particle reactant, in combination with less than an equivalent amount of a substance that will competitively bind with

an antibody analyte, the relative amount of agglutination will determine the concentration of the antibody.

Although Collet-Cassart *et al.* do disclose an agglutination reaction, it is in principle a methodology based on a single particle type whereby the results are obtained by varying concentrations in a competitive binding situation. There is nothing therein that would teach or suggest Applicants' reagent to the person of ordinary skill in the art. Since Lindmo *et al.* and Grange *et al.* cannot be combined in a meaningful way to suggest Applicants' invention as embodied in Claim 22 to the person skilled the art in the absence of a hindsight construction, it is respectfully submitted that Collet-Cassart *et al.,* in spite of the disclosure of testing for CRP, does not add thereto and certainly does not render Claim 22 unpatentable. Withdrawal of the rejection is respectfully requested.

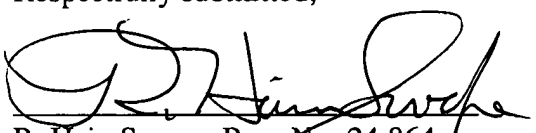
The rejection of Claim 23 under 35 U.S.C. §103 as being unpatentable over Lindmo *et al.*. in view of Grange *et al.*, further in view of Kapmeyer *et al.* is respectfully traversed. That Lindmo *et al.* and Grange *et al.* are not properly combinable and, in fact, teach away from Applicants' invention have been discussed above. Kapmeyer *et al.* teach that PSA is an important analyte and disclose that they have developed a test therefore based on light scattering. However, there is nothing to suggest to one of ordinary skill in the art a diagnostic test comprising Applicants' novel reagent having PSA as the analyte, since Applicants' reagent is neither taught nor suggested by Lindmo *et al.* and Grange *et al.* individually, or in any order. The invention embodied in Claim 23 is certainly not to be found in the suggestion that one might incorporate the particles of Grange *et al.* into the reagent of Lindmo *et al.* if "per chance" if might be used in an agglutination assay, for which the large particles of Lindmo *et al.* would be totally unsuited, regardless of the nature of the analyte. Withdrawal of the rejection is respectfully requested.

Accordingly, it is respectfully submitted that, as Claims 1-4, 6, 9, 10, 20, 22 and 23 clearly define patentable subject matter over the citations cited of record, this application is in condition for allowance. An early Notice of Allowance is courteously solicited.

In the event the Examiner deems a further discussion of this application would expedite prosecution to allowance, the undersigned Attorney of Record would welcome the opportunity to hold such a discussion. The Examiner's cooperation in this regard would be greatly appreciated.

Please address all correspondence to Customer No.: 26345. All telephone calls should be made directly to R. Hain Swope at 973-596-4905. If there are any fees due in respect to this reply, please charge them to Gibbons, Del Deo, Dolan, Griffinger & Vecchione Deposit Account No. 03-3839.

Respectfully submitted,



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